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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,559	08/20/2001	Veerappa S. Subramanian	4961-5	6556

7590 09/04/2002

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/04/2002 3

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,559	SUBRAMANIAN ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☒ Claim(s) 6 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

1. Claim 6 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 6 is dependent upon claim 5 which recite a concentration of carboxyvinyl polymer and its use in the compound. Claim 6 that is dependent from claim 5, only recite the same concentration and recites no further limitations.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 1, 3, 4 and 10 – 13 are rejected under 35 U.S.C. 102(a) as being anticipated by Apelian et al (USPN 6153223). The claims are drawn to a solid dosage form comprising bupropion hydrochloride, carboxyvinyl polymer and an excipient. The excipient is either lactose or microcrystalline cellulose. The dosage form is stabilized and contains 90% w/w of the bupropion HCl after 3 months of storage at 40 degrees Celsius and 7% humidity. The composition comprises between 0.5 and 30 % w/w carboxyvinyl polymer and is used as a stabilizer.

Apelian et al discloses a stabilized solid dosage form of bupropion HCl comprising carboxyvinyl polymer and microcrystalline cellulose or lactose (col. 6, lin. 13 – 27; col. 9, lin. 12 – 33). Also , after testing it was found that after 3 months of storage at 40 degrees Celsius and 75% humidity, 98.9% of the original agent was present (Example F). These disclosures along with others render the claims anticipated.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1 – 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Apelian et al (USPN 6153223) in view of Seth (USPN 6033686). The claims are again drawn to a solid dosage form of bupropion HCl. The dosage form is a sustained release tablet and the composition comprises carboxyvinyl polymer and microcrystalline cellulose or lactose. In addition the stabilization profile discussed above, after 2 weeks of storage at 55 degrees Celsius,

there is at least 90% w/w of the bupropion remaining in the composition. The carboxyvinyl polymer provides a release profile where the drug is released from a period of 8 to 24 hours. Applicant recites a specific profile where the drug is release in a particular percentage at a particular time (i.e. 30 – 45% within 1 hour, 60 – 80% in 4 hours, etc.). Claim 9 recites a method of stabilizing the drug comprising combining the constituents, and granulating with purified water.

As discussed above Apelian discloses essential elements of the claimed invention. In addition to these disclosures, suggests elements of claims 2, 5 – 8 and 14 – 17. First the reference differs from the claimed invention in that it conducts its storage experiments at lower temperature than those of applicant. Yet the conditions for the long-term experiment were identical, and yielded comparable results (Example F). It could be assumed by one of ordinary skill in the art, that a compound that performed similarly in longer range testing would yield similar results in short-term testing as well. It is the position of the examiner that the compound of Apelian obviates that of applicant, and is not patentably distinct from the prior art. Burden is shifted to applicant to show how the compound of the instant invention is patentably distinct from the prior art.

With regard to claims 5 – 8 and 14 – 17, which recite concentrations of the carboxyvinyl polymer and a specific release profile, Apelian suggests these limitations. Apelian is silent to the specific release profile of the compound, yet it does disclose that the formulation is a sustained release tablet comprising carboxyvinyl polymer, bupropion and microcrystalline cellulose or lactose. The reference also discloses that the composition comprises between 10 and 30% w/w

of the vinyl polymer. The reference is however silent to a specific release profile as recited by claims 14 – 17.

Apelian discloses sustained release tablet with all of the general components of applicant. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *In re Russell*, 439 F.2d 1228, 169 USPQ 426 (CCPA 1971).

Seth however discloses a sustained release tablet comprising bupropion HCl, a water insoluble, water-permeable film-forming polymer and water-soluble polymer. The tablet releases 30 – 60% of the bupropion HCl after 1 hour, 55 – 80% after 2 hours, 75 – 95% after 3 hours, and 80 – 100% after 4 hours (col. 3, lin. 40 – 56). Seth also discloses a method of preparing the composition comprising mixing the constituents and granulating with purified water (examples). Though the reference does not explicitly claim this process as stabilizing, Seth's final product is a stable tablet.

With this in mind, on of ordinary skill in the art would have been motivated to follow the suggestions of Seth and Apelian. A skilled artisan would have been motivated follow the suggestions of Seth to use a water-soluble polymer in combination with bupropion HCl in order

to impart the specific release profile of Seth onto the formulation of Apelian. Both reference disclose the same general combination of bupropion HCl, water-insoluble polymers, and water-soluble polymers. The artisan also would have been motivated to apply the processing steps of Seth onto the composition of Apelian, in order to stabilize the composition and produce tablets. A skilled artisan also would have been motivated to assume that the short-term storage properties would be better than the long-term storage properties. It would have been obvious to one of ordinary skill in the art, at the time of the invention to follow these suggestions and teachings in the art with an expected result of a sustained release tablet comprising stabilized bupropion HCl, a vinyl polymer and an excipient with an optimized release profile and storage properties.

Conclusion

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Baker et al (USPN 4687660) and Ruff et al (USPN 5541231) both disclose bupropion HCl sustained release tablets comprising water-soluble polymers.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:30am-4: 30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-7648 for regular communications and 703-746-7648 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Micah-Paul Young
Examiner
Art Unit 1615

MPY
August 27, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600